Substituent Effects on the Intramolecular Cyclization of Dibenzoguanidine Precursors: A Computational Study

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The intramolecular cyclisation that leads to dibenzoguanidine frameworks is a key step in the synthesis of rigid receptors for anion recognition. Previous experimental work showed that conversion of intermediate **1** to compound **2** (Figure 1) occurs only after reduction to a more reactive triamine, highlighting the importance of both electronic factors and molecular preorganization [1].

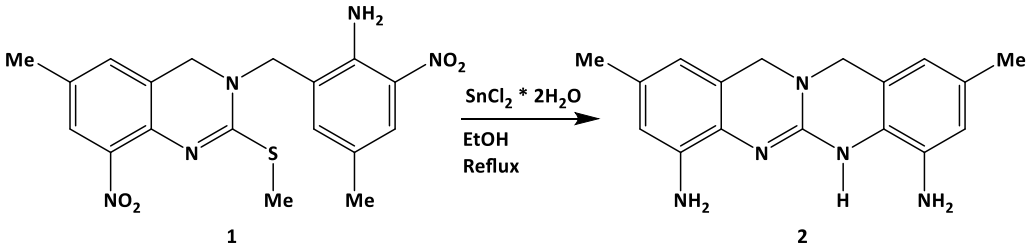

Figure 1. The intramolecular cyclization.

In our work, we attempted to carry out this cyclization using an unsubstituted system (R = H at the 2,9-positions). However, synthesis of compound **2** under these conditions was unsuccessful, indicating that the absence of substituents significantly affects the reaction outcome. This observation prompted a detailed computational investigation.

Density functional theory (DFT) calculations (M062X/6-31G* level of theory) were employed to locate and analyze transition states for a series of substituted systems (R = H, CH_3, Ph,...). Particular attention was given to how electronic effects and steric constraints influence activation barriers and transition-state geometries.

This study aims to provide insight into substituent-controlled intramolecular reactivity, with emphasis on the interplay between nucleophilicity and conformational preorganization, and to support the rational design of preorganized guanidine-based systems.

References:

[1] J.-L. Chicharro, P. Prados, J. de Mendoza, *J. Chem. Soc., Chem. Commun.* (1994) 1193–1194.